AIDS

FIRST REPORTED USE OF ZIDOVUDINE FOR PREVENTION OF PERINATAL HIV TRANSMISSION IN A PREMATURE NEONATE ON ECMO

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Running head: Zidovudine in neonate on ECMO

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Background

The effects of extra corporal membrane oxygenation (ECMO) on pharmacokinetics (PK) of drugs is difficult to predict. Generally, an increased volume of distribution, decreased drug elimination, and sequestration of the drug to the ECMO circuit are factors potentially influencing the PK of drugs during ECMO.[1, 2] Zidovudine is the only antiretroviral agent suitable for intravenous use in newborns for the prevention of perinatal HIV transmission. No reported cases of the influence of ECMO on the PK of zidovudine in prematures were found. We describe the first PK data in a premature neonate requiring intravenous zidovudine while on ECMO.

Case presentation

A premature child (gestational age 32 weeks) born from a virologically suppressed HIV infected mother required ECMO to undergo the resection of an intrathoracic lesion compromising the lungs. IV zidovudine was administered for the prevention of HIV transmission as per standard guidelines. To cope with the anticipated increased volume of distribution (V_d) and in order to avoid the risks caused by under treatment, IV zidovudine was dosed 9mg/kg/day (150% of the dose normally used in premature infants) for the duration of ECMO. Plasma samples were taken before, during and after ECMO. Samples were analysed using LC-MS technology. Therapeutic drug monitoring (TDM) was used to observe treatment and PK parameters were calculated using non-compartmental analysis in WinNonlin. Parents consented to the presentation of these data.

With clearance 0.62 L/h, V_d 3.3 L, and $t_{½}$ of 3.6 h, zidovudine concentrations remained above 0.8mg/L during ECMO (Figure 1). While pharmacokinetic reports on prematures are highly variable with no Ctroughs or AUCs reported, these PK parameters suggest slow clearance of zidovudine, leading to a degree of exposure that has been correlated to increased safety risks in earlier studies.[3] No adverse events were reported in this case and zidovudine levels returned to normal on standard doses after ECMO cessation.[4, 5] The HIV proviral DNA PCR in the child was negative at 3 months of age.

Learning Points/Discussion

It might be difficult to tease out the influence of ECMO versus the premature age on the PK of zidovudine in this particular child. However, the fact that, after ECMO PK parameters of zidovudine were normal after administering normal doses while they were higher during ECMO at a higher dose of zidovudine, suggests that ECMO does not have a major impact on zidovudine PK. Therefore, we recommend that in future occasions, standard IV dosing of zidovudine in premature children on ECMO is recommended under the guidance of TDM.

Acknowledgements

ME initiated the PK study, wrote the report and obtained consent. HW conducted the PK analysis, and wrote the report. AC and DB assisted in the interpretation of results. AP collected clinical data and processed samples. All authors contributed to writing of the report.

References

1. Lequier L. **Extracorporeal life support in pediatric and neonatal critical care: a review**. *J Intensive Care Med* 2004; 19(5):243-258.

2. Mehta NM, Halwick DR, Dodson BL, Thompson JE, Arnold JH. **Potential drug sequestration during extracorporeal membrane oxygenation: results from an ex vivo experiment**. *Intensive Care Med* 2007; 33(6):1018-1024.

3. Balis FM, Pizzo PA, Murphy RF, Eddy J, Jarosinski PF, Falloon J, et al. **The pharmacokinetics of zidovudine administered by continuous infusion in children**. *Ann Intern Med* 1989; 110(4):279-285.

4. Mirochnick M, Capparelli E, Connor J. **Pharmacokinetics of zidovudine in infants: a population analysis across studies**. *Clin Pharmacol Ther* 1999; 66(1):16-24.

5. Pacifici GM. **Pharmacokinetics of antivirals in neonate**. *Early Hum Dev* 2005; 81(9):773-780.

Figure legend

Figure 1. Zidovudine (AZT) levels post dosing

● Zidovudine levels with iv medication, no ECMO

□ Zidovudine levels with iv medication on ECMO

Figure